# PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

## PCT

### NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

| | |
|---|---|
| **Date of mailing** (day/month/year)<br>30 May 2001 (30.05.01) | |
| **International application No.**<br>PCT/US00/12251 | **Applicant's or agent's file reference**<br>GM50053 |
| **International filing date** (day/month/year)<br>04 May 2000 (04.05.00) | **Priority date** (day/month/year)<br>07 May 1999 (07.05.99) |
| **Applicant**<br>BROWN, James, R. et al | |

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

08 November 2000 (08.11.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

**The International Bureau of WIPO**
**34, chemin des Colombettes**
**1211 Geneva 20, Switzerland**

Facsimile No.: (41-22) 740.14.35

Authorized officer

Zakaria EL KHODARY

Telephone No.: (41-22) 338.83.38

US0012251

PATENT COOPERATION TREATY

# PCT



## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

**(PCT Article 36 and Rule 70)**

| Applicant's or agent's file reference GM50053 | FOR FURTHER ACTION | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
|---|---|---|
| International application No. PCT/US00/12251 | International filing date *(day/month/year)* 04 MAY 2000 | Priority date *(day/month/year)* 07 MAY 1999 |
| International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet. | | |
| Applicant SMITHKLINE BEECHAM CORPORATION | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

   I ☒ Basis of the report

   II ☐ Priority

   III ☒ Non-establishment of report with regard to novelty, inventive step or industrial applicability

   IV ☐ Lack of unity of invention

   V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI ☐ Certain documents cited

   VII ☐ Certain defects in the international application

   VIII ☐ Certain observations on the international application

| Date of submission of the demand | Date of completion of this report |
|---|---|
| 08 NOVEMBER 2000 | 16 APRIL 2001 |
| Name and mailing address of the IPEA/US<br>Commissioner of Patents and Trademarks<br>Box PCT<br>Washington, D.C. 20231<br>Facsimile No. (703) 305-3230 | Authorized officer<br>TEKCHAND SAIDHA<br>Telephone No. (703) 308-0196 |

Form PCT/IPEA/409 (cover sheet) (July 1998)*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/12251

## I. Basis of the report

1. With regard to the **elements** of the international application:*

[X] the international application as originally filed

[X] the description:
pages 1-39 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the claims:
pages 40-53 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the drawings:
pages 1-6 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the sequence listing part of the description:
pages 1-6 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[X] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE

[X] the claims, Nos. NONE

[X] the drawings, sheets/~~fig~~ NONE

5. [ ] This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/12251

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. 13, 15, 17-20

because:

☐ the said international application, or the said claim Nos. _ relate to the following subject matter which does not require international preliminary examination *(specify)*.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _ are so unclear that no meaningful opinion could be formed *(specify)*.

☐ the claims, or said claims Nos. _ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 13, 15, 17-20 .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/12251

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. statement

| | | | |
|---|---|---|---|
| Novelty (N) | Claims | 1-12, 14, 16, 21-42 | YES |
| | Claims | NONE | NO |
| Inventive Step (IS) | Claims | 1-12, 14, 16, 21-42 | YES |
| | Claims | NONE | NO |
| Industrial Applicability (IA) | Claims | 1-12, 14, 16, 21-42 | YES |
| | Claims | NONE | NO |

2. citations and explanations (Rule 70.7)

Claims 1-12, 14, 16 and 21-42 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the claimed isolated polynucleotide, vector, host cell and method of making the polypeptide, or antagonists that inhibit the polypeptide expression, or the methods associated with the novel polypeptide or inhibitor compounds. O'Connell et al. teach aroA gene of Staphylococcus encoding an EPSP synthase. The claimed Streptoccoccus pnemoniae DNA sequence encoding the amino acid sequence of SEQ ID NO : 2 having 70 % homology or methods based upon the sequences,is outside the range of teachings of O'Connell et al.

Claims 1-12, 14, 16 and 21-42 meet the criteria set out in PCT Article 33(4), because the subject matter claimed can be made or used in industry.

---------- NEW CITATIONS ----------

O'CONNELL et al. Sequence and Mapping of the aroA gene of Staphyloccoccus aureus 8325-4. Journal of General Microbiology. 1993, Vol. 139, pages 1449-1460, see the entire document.

MAJUMDER et al. 5-Enolpyruvylshikimate-3-phosphate synthase of Bacillus subtilis is an allosteric enzyme. Eur. J. Biochem. 1995, Vol. 229, pages 99-106, see the entire document.

**Supplemental Box**
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII



CLASSIFICATION:
The International Patent Classification (IPC) and/or the National classification are as listed below:
IPC(7): CO7H 21/04; C12P 21/06; C12N 1/20, 15/00 and US Cl.: 536/23.1, 23.7; 435/69.1, 69.2, 252.3, 320.1

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 :
C07H 21/04, C12P 21/06, C12N 1/20, 15/00

A1

(11) International Publication Number: WO 00/68243

(43) International Publication Date: 16 November 2000 (16.11.00)

(21) International Application Number: PCT/US00/12251

(22) International Filing Date: 4 May 2000 (04.05.00)

(30) Priority Data:
60/133,070 7 May 1999 (07.05.99) US

(71) Applicants *(for all designated States except US)*: SMITHKLINE BEECHAM CORPORATION [US/US]; One Franklin Plaza, Philadelphia, PA 19103 (US). SMITHKLINE BEECHAM PLC [GB/GB]; New Horizons Court, Great West Road, Brentford, Middlesex TW8 9EP (GB).

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(74) Agents: GIMMI, Edward, R. et al.; SmithKline Beecham Corporation, Corporate Intellectual Property, UW2220, 709 Swedeland Road, P.O. Box 1539, King of Prussia, PA 19406-0939 (US).

(81) Designated States: JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
*With international search report*

(54) Title: METHODS USING MECHANISMS OF ACTION OF AROA

(57) Abstract

The invention provides aroA polypeptides and DNA (RNA) encoding aroA polypeptides and methods for producing such polypeptides by recombinant techniques. Also provided are methods for utilizing aroA polypeptides to screen for antibacterial compounds.

*FOR THE PURPOSES OF INFORMATION ONLY*

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
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| CM | Cameroon | | | PL | Poland | | |
| CN | China | KR | Republic of Korea | PT | Portugal | | |
| CU | Cuba | KZ | Kazakstan | RO | Romania | | |
| CZ | Czech Republic | LC | Saint Lucia | RU | Russian Federation | | |
| DE | Germany | LI | Liechtenstein | SD | Sudan | | |
| DK | Denmark | LK | Sri Lanka | SE | Sweden | | |
| EE | Estonia | LR | Liberia | SG | Singapore | | |

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00 12251

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) :C07H 21/04; C12P 21/06; C12N 1/20, 15/00
US CL :536/23.1, 23.7; 435/69.1, 69.2, 252.3, 320.1

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.1, 23.7; 435/69.1, 69.2, 252.3, 320.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

West and STN files : medline, caplus, uspatfull, biosis, scisearch - search terms : aroA gene? and streptococcus pheumoniae.

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X,P | US 5,883,239A (BROWN ET AL.) 16 March 1999 (16.3.1999), see entire document, especially the abstract. | 1-12, 14, 16, 21-42 |

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 25 JULY 2000 | 10 AUG 2000 |
| Name and mailing address of the ISA/US<br>Commissioner of Patents and Trademarks<br>Box PCT<br>Washington, D.C. 20231<br>Facsimile No. (703) 305-3230 | Authorized officer<br>TEKCHAND SAIDHA<br>Telephone No. (703) 308-0196 |

Form PCT/ISA/210 (second sheet) (July 1998)★

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/12251

**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
1-12, 14, 16 & 21-42

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/12251

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING
This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.
Group I, claim(s)1-12, drawn to polynucleotide encoding aroA polypeptide, vector host cells and method of making the polypeptide.
Group II, claim(s)13, drawn to antibody against the polypeptide of claim 11.
Group III, claim(s)14, 16 & 21-42, drawn to antagonists and method of use.
Group IV, claim(s) 15 drawn to a method of treatment using aroA.
Group V, claim(s) 17, drawn to Process of diagnosing a disease.
Group VI, claim(s) 18, drawn to polypeptide inhibitors
Group VII, claims 19-20, drawn to a method of inducing an immonological response.
The inventions listed as Groups 1-VII do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The Polynucleotide of Group I and the antibody of Group II do not require each other for their practice, have separate utilities, such as the polynucleotide of Group I can be used for recombinant expression of the aroA polypeptide versus the use of antibody to detect proteins. Group I has a special technical feature of nucleotide sequence encoding aorA which Groups II-VII do not share; Group II has the special technical feature of an antibody which Group I and III-VII do not share. Group III has the special technical feature of an antagonist, which Groups I-II and Groups IV-VII do not share; Group IV has the special technical feature of an a treatment based upon aroA polypeptide, which Groups I-III and Groups V-VII do not share; Group V has the special technical feature of a process for diagnosis of disease based upon expression of protein, which Groups I-IV and Groups VI-VII do not share; Group VI has the special technical feature of an of a method for identifying compounds which inhibit polypeptide activity, which Groups I-V and Groups VII do not share; Group VII has the special technical feature of a method for inducing an immunological response, which Groups I-VI do not share.

SEQUENCE LISTING

<110> SMITHKLINE BEECHAM CORPORATION
SMITHKLINE BEECHAM plc

<120> METHODS USING MECHANISMS OF ACTION OF AroA

<130> GM50053

<140> TO BE ASSIGNED
<141> 2000-05-04

<150> US 60/133,070
<151> 1999-05-07

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Gly Glu His Val Leu Ser Thr Met Gln Val Phe Arg Asp Leu Gly Val
        35                  40                  45
Glu Ile Glu Asp Lys Asp Gly Val Ile Thr Val Gln Gly Val Gly Met
    50                  55                  60
Ala Gly Leu Lys Ala Pro Gln Asn Ala Leu Asn Met Gly Asn Ser Gly
65                  70                  75                  80
Thr Ser Ile Arg Leu Ile Ser Gly Val Leu Ala Gly Ala Asp Phe Glu
                85                  90                  95
Val Glu Met Phe Gly Asp Asp Ser Leu Ser Lys Arg Pro Met Asp Arg
            100                 105                 110
Val Thr Leu Pro Leu Lys Lys Met Gly Val Ser Ile Ser Gly Gln Thr
        115                 120                 125
Glu Arg Asp Leu Pro Pro Leu Arg Phe Lys Arg Asp Glu Lys Pro Lys
    130                 135                 140
Thr Tyr Ser Leu Xaa Val Ala Asn Cys Leu Cys Pro Ser Gln Val Ser
145                 150                 155                 160
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Lys Gly Glu Ser Val Ile Ile Glu
                165                 170                 175
Lys Glu Tyr Thr Arg Asn His Thr Glu Asp Met Leu Gln Gln Phe Gly
            180                 185                 190
Gly His Leu Ser Val Asp Gly Lys Lys Ile Thr Val Gln Gly Pro Gln
        195                 200                 205
Lys Leu Thr Gly Gln Lys Val Val Val Pro Gly Asp Ile Ser Ser Ala
    210                 215                 220
Ala Phe Trp Leu Val Ala Gly Leu Ile Ala Pro Asn Ser Arg Leu Val
225                 230                 235                 240
Leu Gln Asn Val Gly Ile Asn Glu Thr Arg Thr Gly Ile Ile Asp Val
                245                 250                 255
Ile Arg Ala Met Gly Gly Lys Leu Glu Ile Thr Glu Ile Asp Pro Val
            260                 265                 270
Ala Lys Ser Ala Thr Leu Ile Val Glu Ser Ser Asp Leu Lys Gly Thr
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Glu Ile Cys Gly Ala Leu Ile Pro Arg Leu Ile Asp Glu Leu Pro Ile
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305                 310                 315                 320
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Met Ile Ile Lys Gly Lys Ser Ala Leu His Gly Ala Arg Val Asn Thr
        355                 360                 365
Phe Gly Asp His Arg Ile Gly Met Met Thr Ala Ile Ala Ala Leu Leu
    370                 375                 380
Val Ala Asp Gly Glu Val Glu Leu Asp Arg Ala Glu Ala Ile Asn Thr
385                 390                 395                 400
Ser Tyr Pro Ser Phe Phe Asp Asp Leu Glu Ser Leu Ile His Gly
                405                 410                 415
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